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ORIGINAL ARTICLE

Observational Study

Cerebral perfusion in patients with unilateral internal carotid artery occlusion by dual post-labeling delays arterial spin labeling imaging

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Abstract

BACKGROUND

Global and regional cerebral blood flow (CBF) changes in patients with unilateral internal carotid artery occlusion (ICAO) are unclear when the dual post-labeling delays (PLD) arterial spin labeling (ASL) magnetic resonance imaging (MRI) technique is used. Manual delineation of regions of interest for CBF measurement is time-consuming and laborious.

AIM

To assess global and regional CBF changes in patients with unilateral ICAO with the ASL-MRI perfusion technique.

METHODS

Twenty hospitalized patients with ICAO and sex- and age-matched controls were included in the study. Regional CBF was measured by Dr. Brain's ASL software. The present study evaluated differences in global, middle cerebral artery (MCA) territory, anterior cerebral artery territory, and Alberta Stroke Program Early Computed Tomography Score (ASPECTS) regions (including the caudate nucleus, lentiform nucleus, insula ribbon, internal capsule, and M1-M6) and brain lobes (including frontal, parietal, temporal, and insular lobes) between ICAO patients and controls at PLD 1.5 s and PLD 2.5 s.

RESULTS

When comparing CBF between ICAO patients and controls, the global CBF in ICAO patients was lower at both PLD 1.5 s and PLD 2.5 s; the CBF on the occluded side was lower in 15 brain regions at PLD 1.5 s, and it was lower in 9 brain regions at PLD 2.5 s; the CBF in the contralateral hemisphere was lower in the caudate nucleus and internal capsule at PLD 1.5 s and in M6 at PLD 2.5 s. The global CBF in ICAO patients was lower at PLD 1.5 s than at PLD 2.5 s. The ipsilateral CBF at PLD 1.5 s was lower than that at PLD 2.5 s in 15 regions, whereas

the contralateral CBF was lower at PLD 1.5 s than at PLD 2.5 s in 12 regions. The ipsilateral CBF was lower than the contralateral CBF in 15 regions at PLD 1.5 s, and in M6 at PLD 2.5 s.

CONCLUSION
Unilateral ICAO results in hypoperfusion in the global and MCA territories, especially in the ASPECTS area. Dual PLD settings prove more suitable for accurate CBF quantification in ICAO.

Key Words: Arterial spin labeling; Internal carotid artery occlusion; Ischemic stroke; Cerebral blood flow; Hemodynamic

Core Tip: In this study, the dual post-labeling delays (PLD) arterial spin labeling (ASL) technique was used for cerebral blood flow (CBF) imaging in unilateral internal carotid artery occlusion (ICAO) patients. Intelligent ASL analysis software was used for rapid quantification of regional CBF, including the Alberta Stroke Program Early Computed Tomography Score (ASPECTS) regions. A comparison with the controls suggests that unilateral ICAO resulted in hypoperfusion in the global and middle cerebral artery territory, affecting most of the ASPECTS area on the occluded side and a small part of the ASPECTS area on the nonoccluded side. The dual PLD settings are more suitable for accurate CBF quantification in ICAO.

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INTRODUCTION

Internal carotid artery occlusion (ICAO) is less common but still significant for the etiology of transient ischemic attack (TIA) and cerebral infarction[1]. Atherosclerosis is the major contributing etiology[2]. ICAO diminishes the perfusion pressure on the occluded side, potentially leading to blood redistribution from the contralateral ICA or posterior circulation, along with collateral blood flow towards the affected hemisphere[3]. ICAO patients exhibit ischemic symptoms involving the middle cerebral artery (MCA) and/or anterior cerebral artery (ACA) territories in the anterior circulation[4]. Therefore, assessing changes in global and regional cerebral blood flow (CBF) within the ACA and MCA territories is crucial.

Previous studies have predominantly used single post-labeling delay (PLD) or manual region-of-interest selection for CBF measurement, but these approaches are time-consuming and labor-intensive. Leveraging advances in artificial intelligence, Dr. Brain's software enables the automatic calculation of global and anatomical regional CBF. This facilitates easier adoption of advanced magnetic resonance imaging (MRI) technology for patient diagnosis and monitoring.

The Alberta Stroke Program Early Computed Tomography Score (ASPECTS) serves as a straightforward and reliable qualitative scoring system widely used to assess early ischemic cerebral infarction severity. It plays a critical role in decision-making in endovascular treatment (EVT)[5-8], assisting in treatment prediction and prognosis. However, a notable gap in perfusion research focused on ASPECTS regions remains.

This retrospective study aims to analyze global and regional CBF changes in unilateral atherosclerotic ICAO patients with the aforementioned tools.

MATERIALS AND METHODS

Subjects

The hospital ethics committee approved the current retrospective study, and informed consent was obtained from all the participants. Between September 2021 and March 2024, patients who were diagnosed with unilateral ICAO confirmed by digital subtraction angiography and who underwent dual PLDs ASL imaging were included. The exclusion criteria were as follows: (1) Moderate or severe stenosis (≥ 50%) in contralateral vessels; (2) Poor image quality or ASL with single or other PLD; and (3) Brain injury, a history of brain surgery, psychiatric disorders, or other conditions affecting brain function. The patient enrolment process is illustrated in Figure 1.

Finally, twenty functionally independent ICAO patients (three women and seventeen men; mean age: 57.50 ± 10.841 years) and sex- and age-matched control subjects were examined.

All stroke patients had an ASPECTS score of 8-10 on diffusion weighted imaging (DWI), and the infarctions were located in the MCA territory. All stroke patients had subcortical watershed infarctions, 2 of them had cortical infarctions, and one of which with a basal area infarction. None of the patients presented infarct lesions exceeding 30 mm in diameter in the territory ipsilateral to the ICA occlusion.

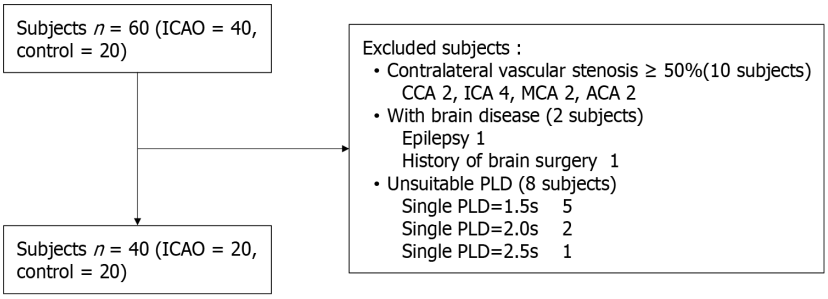

Figure 1 Study enrollment showing exclusion criteria. CCA: Common carotid artery; ICA: Internal carotid artery; MCA: Middle cerebral artery; ACA: Anterior cerebral artery; ICAO: Internal carotid artery occlusion; PLD: Post-labeling delay.

MRI

The ASL and DWI sequences were scanned with a 3.0T scanner (HDxt Signa; GE Healthcare) outfitted with an 8-channel head coil for signal acquisition. A three-dimensional pseudo-continuous ASL (PCASL) sequence was used for the whole brain. The parameters of ASL were as follows: Repetition time (TR) 4599 ms (PLD 1525 ms), TR5294 ms (PLD 2525 ms), echo time (TE) 10.86 ms, labelling duration 1500 ms, field of view (FOV) 24 cm × 24 cm, layer thickness 4.0 mm, 36 slices, with background suppression. The parameters of DWI were as follows: TR, 5500 ms; TE, 75 ms; FOV, 22 cm × 22 cm; and layer thickness, 5.0 mm.

Statistical analysis

The original ASL sequence data (PLD 1.5 s and PLD 2.5 s were anonymized and uploaded to the Dr. Brain software ASL module (YIWEI Medical Technology, China). The Buxton hemodynamic model was processed with blood T1 and brain tissue T1 constants set at 1650 and 11665 ms, respectively. Figure 2 depicts the processing flow diagram and schematic for brain region segmentation.

This study evaluated differences in regional CBF across several areas: Global, MCA territory; ACA territory; ASPECTS regions (including the caudate nucleus, lentiform nucleus, insula ribbon, internal capsule, and M1-M6); and brain lobes (including the frontal, parietal, temporal, and insular lobes). This analysis compared CBF differences between the ipsilateral and contralateral hemispheres to the occlusion and control subjects at PLD 1.5 s and PLD 2.5 s.

Owing to the absence of differences in CBF between the left and right hemispheres in control subjects, the CBF values for these hemispheres were averaged for analysis.

The Statistical Package for the Social Sciences for Windows, Version 21.0 (SPSS, Chicago), was used for statistical analysis in this study. All measurement data were tested for normality *via* the Shapiro-Wilk test. Data that conformed to a normal distribution and exhibited homogeneous variance are presented as the means ± SD; otherwise, the data are presented as medians (quartile ranges). As the data conformed to a normal distribution and the variance was homogeneous, paired sample or two independent sample *t* tests were used for intergroup comparisons; otherwise, nonparametric Wilcoxon (W) or Mann-Whitney *U* tests were used. Differences were considered significant when $P < 0.05$.

RESULTS

The fundamental features of the ICAO patients are shown in Table 1. Regional CBF data are shown in Table 2.

Differences in regional CBF between ICAO and control group

The global CBF of ICAO patients was significantly lower than that of the control group at PLD 1.5 s (24.152 ± 4.517 *vs* 30.194 ± 7.164 mL/min/100 g, $P = 0.011$) and PLD 2.5 s (28.904 ± 4.564 *vs* 34.028 ± 6.730 mL/min/100 g, $P = 0.024$).

Compared with that of the control subjects, the CBF in the occluded hemisphere was significantly lower in 15 brain regions at PLD 1.5 s ($P < 0.05$), but no differences were found in the ACA territory ($P > 0.05$) (as shown in Table 3). The CBF in the occluded hemisphere was lower in the MCA territory, insula ribbon, M2, M3, M4, M5, M6, parietal lobe ($P < 0.05$), and temporal lobe at PLD 2.5 s ($P < 0.05$), but no differences were found in the ACA territory, caudate nucleus, lentiform nucleus, internal capsule, M1, frontal lobe, or insular lobe ($P > 0.05$) (as shown in Table 3).

Compared with that of the control subjects, the CBF in the contralateral hemisphere was significantly lower in the caudate nucleus and internal capsule at PLD 1.5 s ($P < 0.05$), but no differences were found in the other 14 brain regions ($P > 0.05$) (as shown in Table 3). The CBF in the contralateral hemisphere was lower in M6 at PLD 2.5 s ($P < 0.05$), but no differences were found in the other 15 brain regions ($P > 0.05$) (as shown in Table 3).

Differences in regional CBF between PLD 1.5 s and PLD 2.5 s

The global CBF at PLD 1.5 s was significantly lower than that at PLD 2.5 s (24.152 ± 4.517 *vs* 28.904 ± 4.564 mL/min/100 g, $P = 0.000$).

Table 1 Patient characteristics of internal carotid artery occlusion

Patient Number	Age (year)	Sex	Symptoms/Onset time	Imaging	Occlusion side	Occlusion site	Contralateral side	Collateral flow pathway
1	47	Female	Headache/1 month		R	Initial		ACoA
2	51	Male	Neuro-deficiency/5 days	Stroke	R	Ophthalmic		ACoA
3	50	Male	Neuro-deficiency/1 week	Stroke	R	Ophthalmic		ACoA + PCoA + L
4	57	Male	Neuro-deficiency/1 week	Stroke	L	Initial		ACoA + PCoA + OA
5	58	Male	TIA/4 days		R	Initial	CCA 20%	ACoA + L + OA
6	55	Male	Neuro-deficiency/2 weeks	Stroke	R	Clinoid		OA
7	82	Male	TIA/1 month		L	Initial	ICA 20%	ACoA + PCoA
8	67	Male	Neuro-deficiency/4 days	Stroke	L	Initial	ICA 20%	ACoA
9	66	Male	Neuro-deficiency/2 weeks	Stroke	R	Initial	ICA 20%	PCoA
10	61	Female	Headache/2 months		L	Ophthalmic		ACoA + PCoA + L
11	56	Male	Dizziness/1 month	Stroke	R	Initial	MCA 20%	ACoA + PCoA + OA
12	57	Male	Dizziness/3 years		L	Communicating	ICA 20%	PCoA
13	42	Male	Dizziness/3 days		L	Ophthalmic		ACoA + PCoA
14	59	Male	TIA/1 week		R	Initial	ICA 20%	ACoA + PCoA + OA + L
15	35	Male	Neuro-deficiency/2 months	Stroke	R	Terminal		New vessels + L
16	70	Male	Neuro-deficiency/2 months	Stroke	R	Ophthalmic	ICA 20%-30%	ACoA + PCoA
17	46	Female	Neuro-deficiency/5 days	Stroke	R	Ophthalmic		ACoA
18	62	Male	TIA/3 days		L	Initial	ICA 40%	OA
19	71	Male	Neuro-deficiency/10 days	Stroke	L	Initial	ICA 40%	
20	58	Male	Neuro-deficiency/3 days	Stroke	L	Ophthalmic	ICA 20%	ACoA

CCA: Common carotid artery; TIA: Transient ischemic attack; ICA: Internal carotid artery; MCA: Middle cerebral artery; ICA: Internal carotid artery; MCA: Middle cerebral artery; ACA: Anterior cerebral artery; ACoA: Anterior communicating artery; PCoA: Posterior communicating artery; OA: Ophthalmic artery; L: Leptomeningeal.

When comparing PLD 1.5 s with PLD 2.5 s, the CBF on the occluded side was significantly lower in 15 brain regions ($P < 0.05$), but no differences were found in the internal capsule ($P > 0.05$) (as shown in Table 3). The CBF of the nonoccluded side was significantly lower in 12 brain regions ($P < 0.05$), but no differences were found in the caudate nucleus, lentiform nucleus, insula ribbon, or M2 region ($P > 0.05$) (as shown in Table 3).

Differences in regional CBF between ipsilateral and contralateral to the ICAO

At PLD 1.5 s, the CBF in 15 brain regions ipsilateral to the ICAO was significantly lower than that in the contralateral hemisphere ($P < 0.05$), but no differences were found in the ACA territory ($P > 0.05$) (as shown in Table 3).

At PLD 2.5 s, the CBF in the M6 region ipsilateral to the ICAO was significantly lower than that in the contralateral hemisphere ($P < 0.05$), but no differences were found in the other 15 brain regions at PLD 2.5 s ($P > 0.05$) (as shown in Table 3).

Table 2 The regional cerebral blood flow value, mean ± SD/ Median (quartile)

Variables brain region	Ips-CBF at PLD 1.5	Ips-CBF at PLD 2.5	Con-CBF at PLD 1.5	Con-CBF at PLD 2.5	HC CBF at PLD 1.5	HC CBF at PLD 2.5
Anterior	27.968 ± 7.941	32.687 ± 7.409	29.728 ± 4.828	32.24 (11.3)	33.353 ± 7.966	38.226 ± 6.900
Middle	18.818 ± 6.485	29.09 (6.93)	27.504 ± 4.243	30.71 (4.05)	31.687 ± 7.907	35.710 ± 7.602
Caudate nucleus	17.57 ± 4.573	21.67 ± 5.603	22.175 ± 3.355	23.714 ± 5.898	26.442 ± 4.510	31.393 ± 5.603
Lentiform nucleus	19.812 ± 7.299	25.054 ± 5.531	28.816 ± 4.572	27.412 ± 4.750	33.222 ± 6.785	29.205 ± 6.178
Insula ribbon	24.313 ± 8.122	31.186 ± 5.886	33.001 ± 3.984	32.176 ± 3.502	38.537 ± 8.69	36.881 ± 8.136
Internal capsule	24.464 ± 3.627	24.449 ± 4.307	20.248 ± 5.343	23.861 ± 5.089	29.292 ± 4.519	24.958 ± 4.429
M1	19.764 ± 6.796	28.01 (5.47)	27.172 ± 4.373	29.05 (4.35)	31.417 ± 7.361	33.463 ± 7.962
M2	19.735 ± 9.102	28.088 ± 7.164	31.633 ± 4.568	32.035 (5.61)	37.329 ± 9.097	36.49 ± 8.590
M3	20.208 ± 7.954	29.376 ± 7.442	29.249 ± 6.268	33.245 ± 5.028	32.575 (7.83)	38.132 ± 9.422
M4	19.293 ± 6.837	29.59 (9.53)	25.399 ± 4.554	29.64 (5.81)	28.413 ± 7.149	35.048 ± 6.726
M5	16.271 ± 7.443	25.099 ± 7.604	25.688 ± 5.449	29.03 (4.48)	26.45 (4.22)	33.933 ± 6.944
M6	15.902 ± 6.986	24.869 ± 7.918	25.057 ± 5.284	30.209 ± 3.750	29.28 (5.58)	36.683 ± 7.377
Frontal lobe	19.933 ± 6.746	29.98 (7.99)	27.238 ± 4.513	30.21 (4.62)	30.712 ± 7.051	34.558 ± 7.166
Parietal lobe	19.471 ± 6.988	26.906 ± 7.273	26.378 ± 5.135	30.42 (2.81)	28.698 (4.82)	36.092 ± 6.995
Temporal lobe	19.931 ± 7.940	28.557 ± 7.084	29.646 ± 5.311	32.257 ± 4.582	33.393 ± 8.285	36.518 ± 8.837
Insular lobe	25.732 ± 6.496	32.083 ± 7.257	30.485 ± 4.243	32.29 (6.4)	34.371 ± 7.031	35.689 ± 6.415

Ips: Ipsilateral to internal carotid artery occlusion; Con: Contralateral to internal carotid artery occlusion; HC: Health control; PLD: Post-labeling delay.

DISCUSSION

ASL and dynamic susceptibility contrast (DSC) MRI perfusion imaging are commonly used to measure CBF; DSC requires intravenous bolus administration of gadolinium, while ASL is performed without exogenous contrast and uses arterial blood water as an endogenous diffusible tracer. Owing to current concerns about the use of contrast agents in patients with poor kidney function, an alternative approach with no harmful effects would be highly beneficial. ASL has become the most widely used perfusion imaging sequence in the clinic. ASL labelling approaches include continuous and pulsed labelling, and PCASL provides superior labelling efficiency and is compatible with modern body coil radiofrequency transmission hardware that is recommended for clinical imaging[9].

The labeling duration and PLDs are the most important information that can be used to interpret (quantify) CBF images[10]. ASL permits noninvasive estimation of CBF but relies upon the arterial transit time (ATT)[11]. While ATT is well defined for healthy vasculature, it can clearly differ in disease states, potentially making conventional single PLD ASL techniques unsuitable[12]. Owing to the formation of collateral blood flow, the transit time is prolonged in cerebral artery steno-occlusive diseases, which restricts the accurate measurement of CBF by ASL[12-14]. However, the use of a solitary traditional PLD results in an underestimation of CBF[9,12], which can be partially mitigated by using long PLD [2]. In addition to the PLD of 1.5 seconds, we employed a relatively longer PLD of 2.5 seconds, as seen in previous studies. Akiyama *et al*[11] reported the efficacy of using dual PLDs with 1.5- and 2.5-second techniques to evaluate the slow collateral blood flow that sustains the cerebrovascular reserve (CVR) in stenotic or occlusive ICA conditions[11,15].

Compared with those in the control group and contralateral hemisphere, the current findings indicate that nonacute unilateral atherosclerotic ICAO results in decreased CBF in the global, MCA territory and across most ASPECTS areas of the ipsilateral hemisphere at both PLD 1.5 s and PLD 2.5 s. ICAO leads to the interruption of blood flow on the occluding side. Owing to its anatomical characteristics, the MCA territory is most affected, and the ASPECTS area is located in the MCA territory, so it is also affected. This finding is consistent with previous research; for example, Jeroen Hendrikse's study demonstrated reduced CBF in the grey matter of the ipsilateral MCA territory[16]. Bokkers *et al*[17] reported significantly decreased CBF in the frontal and frontal parietal regions on the occluded side of the ICA[17]. Furthermore, studies using contrast-enhanced perfusion imaging have consistently shown reduced CBF in both grey and white matter of the occluded hemisphere of the ICA[18-20].

The CBF in the ACA territory was not affected in this study, which is inconsistent with previous research. Hartkamp *et al*[3] reported that in patients with ICAO, the CBF was significantly lower in the ACA and MCA territories on the occluded side of the ICA than in control subjects[3]. This may be related to the fact that 70% of the ICAO patients included in this study had anterior communicating artery compensation, and primary collateral circulation can quickly compensate for CBF.

Table 3 Statistical result

Variables brain region	*P* value	*P* value	*P* value	*P* value	*P* value	*P* value	*P* value	*P* value
Anterior	0.088	0.054	0.147	0.095	0.001[e]	0.000[f]	0.454	1.000
Middle	0.000[a]	0.009[b]	0.083	0.078	0.000[e]	0.002[f]	0.000[g]	0.175
Caudate nucleus	0.000[a]	0.176	0.008[c]	0.715	0.001[e]	0.191	0.003[g]	0.323
Lentiform nucleus	0.000[a]	0.073	0.050	0.393	0.000[e]	0.117	0.001[g]	0.206
Insula ribbon	0.000[a]	0.041[b]	0.068	0.073	0.001[e]	0.267	0.003[g]	0.567
Internal capsule	0.004[a]	0.762	0.000[c]	0.557	0.988	0.003[f]	0.014[g]	0.727
M1	0.000[a]	0.063	0.068	0.137	0.000[e]	0.006[f]	0.001[g]	0.546
M2	0.000[a]	0.009[b]	0.246	0.098	0.000[e]	0.577	0.001[g]	0.061
M3	0.001[a]	0.011[b]	0.286	0.088	0.000[e]	0.006[f]	0.001[g]	0.095
M4	0.002[a]	0.014[b]	0.185	0.070	0.000[e]	0.000[f]	0.006[g]	0.291
M5	0.002[a]	0.004[b]	0.577	0.099	0.000[e]	0.000[f]	0.000[g]	0.090
M6	0.000[a]	0.000[b]	0.086	0.005[d]	0.000[e]	0.001[f]	0.000[g]	0.035[h]
Frontal lobe	0.000[a]	0.070	0.124	0.286	0.000[e]	0.000[f]	0.001[g]	0.291
Parietal lobe	0.002[a]	0.002[b]	0.178	0.051	0.000[e]	0.000[f]	0.003[g]	0.152
Temporal lobe	0.000[a]	0.014[b]	0.157	0.109	0.000[e]	0.036[f]	0.000[g]	0.090
Insular lobe	0.002[a]	0.184	0.080	0.286	0.000[e]	0.042[f]	0.002[g]	0.985

[a]$P < 0.01$, ipsilateral *vs* control at post-labeling delay 1.5 s.
[b]$P < 0.05$, ipsilateral *vs* control at post-labeling delay 2.5 s.
[c]$P < 0.01$, contralateral *vs* control at post-labeling delay 1.5 s.
[d]$P < 0.01$, contralateral *vs* control at post-labeling delay 2.5 s.
[e]$P < 0.001$, ipsilateral post-labeling delay 1.5 s *vs* post-labeling delay 2.5 s.
[f]$P < 0.05$, contralateral post-labeling delay 1.5 s *vs* post-labeling delay 2.5 s.
[g]$P < 0.05$, ipsilateral *vs* contralateral at post-labeling delay 1.5 s.
[h]$P < 0.05$, ipsilateral *vs* contralateral at post-labeling delay 2.5 s.

The ASPECTS was originally developed to assess the volume of acute MCA infarction on non-contrast CT scans, but its applicability extends to multimodal MRI techniques as well. In the present study, all cerebral infarction patients had ASPECTS values ranging from 8 to 10. A previous meta-analysis revealed that higher ASPECTS values (8-10) are associated with significantly better outcomes following EVT than lower ASPECTS values[21]. In China, research on acute large-vessel occlusion in the anterior circulation has demonstrated that patients with larger infarctions (ASPECTS scores 3-5 and infarct volume 70-100 mL) benefit more from endovascular therapy than from medical management alone[22].

ASPECTS can be divided into subcortical (including the caudate nucleus, lentiform nucleus, insula ribbon, and internal capsule) and cortical regions (including M1-M6)[23]. The findings of the current study indicate that the hypoperfusion areas in ASPECTS regions are located mainly in the cortex, a detail not previously emphasized. Another study indicated that a higher baseline cortical ASPECTS was predictive of favorable clinical outcomes in patients with ASPECTS < 6 and large vessel occlusion treated with EVT[24]. Therefore, the ASPECTS has significant clinical importance, and perfusion evaluation is necessary.

The CBF at PLD 1.5 s was significantly lower than that at PLD 2.5 s globally, in MCA territories, and in most ASPECTS areas, and the hypoperfusion areas from PLD 1.5 s to PLD 2.5 s were reduced in the occluded hemisphere. These findings indicate the existence of slow flow and redistribution to compensate for ischemia in unilateral ICAO. The current results indicate that the selection of the parameter PLD for ASL can affect the evaluation of CBF correctly because of the presence of slow flow in ICAO patients, and a shorter PLD of 1.5 seconds may result in an underestimation of regional CBF in ICAO patients. An increase in collateral flow in ICAO patients results in longer blood flow pathways and a prolonged blood arrival time[25,26]. A shorter delay does not allow the labelled blood water to be fully delivered to the tissue, and a longer PLD must be included. Our results indicate that dual PLD settings can improve the quantification of CBF in ICAO patients. Presently, many clinical studies have been performed utilizing several PLDs with ATT correction to improve accurate quantification of CBF[12,14,25,26], and the latest work has shown a multi-PLD technique that gauges CBF and ATT, building regional ATT parametric maps to better display pathological tissue[27]. Single-PLD ASL is often sufficient for rapid evaluation of steno-occlusive disease hemodynamics, whereas multi-PLD potentially increases CBF accuracy and provides regional ATT information, and the ATT artefacts can be corrected[10].

Previous studies have shown various findings regarding CBF patterns in the contralateral hemisphere of ICAO patients. For example, one study reported no significant difference in grey matter CBF within the MCA territory between the hemisphere contralateral to the ICAO and a matched control group[16]. Conversely, Bokkers *et al*[17] reported

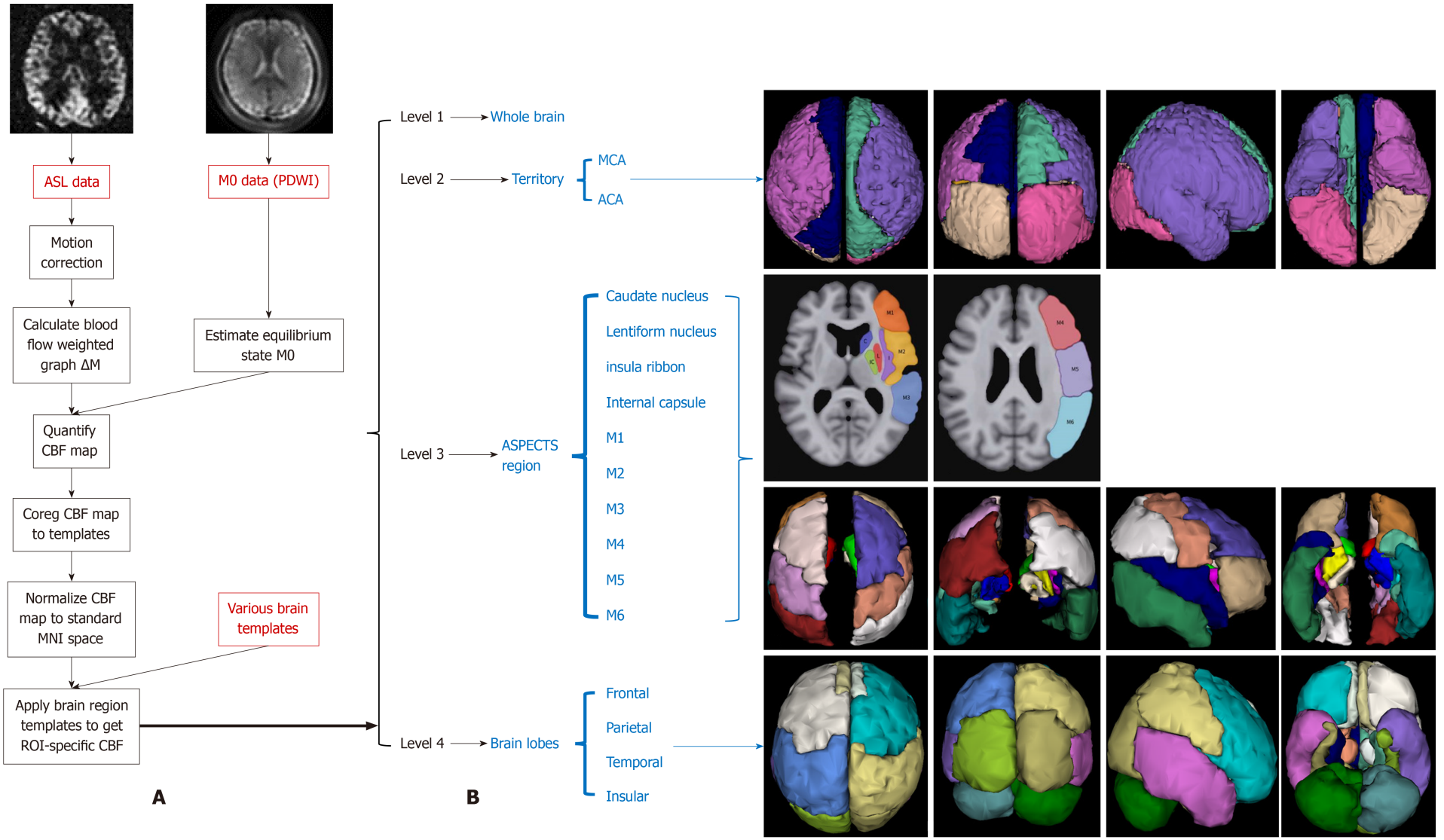

Figure 2 Data processing flow chart and brain segmentation diagram. A: Dr Brain's software arterial spin labeling module processing flow diagram; B: Segmentation brain structure of regions of interest. ASL: Arterial spin labeling; PDWI: Proton density weighted image; CBF: Cerebral blood flow; ROI: Region of interest; ASPECTS: Alberta Stroke Programme Early Computed Tomography Score; MCA: Middle cerebral artery; ACA: Anterior cerebral artery.

significantly lower CBF in the anterior frontal region of the nonoccluded hemisphere in ICAO patients than in controls [17]. Additionally, Hartkamp *et al*[3] demonstrated that the CVR was significantly lower in the ACA and MCA territories of the nonoccluded hemisphere in ICAO patients than in control subjects[13]. Given these discrepancies in previous findings, the results of our current study hold particular significance. We found that the CBF was significantly lower in some ASPECTS areas, such as the lower CBF in the caudate nucleus and internal capsule at PLD 1.5 s and in M6 at PLD 2.5 s, than in the control subjects. Furthermore, we observed that the CBF at PLD 1.5 s was significantly lower than that at PLD 2.5 s. The difference in CBF between PLD 1.5 s and PLD 2.5 s in the contralateral hemisphere represents the existence of slow flow and redistribution to compensate for ischemia. Occlusion of an artery results in a decrease in pressure in that territory, and this pressure gradient will cause blood to flow from healthy arteries to the territory of the occluded artery. Because the collateral blood flow path is long, when the blood flow arrives late, it cannot be detected with a short PLD, and the CBF measured with a long PLD can truly reflect cerebral perfusion. These findings suggest that unilateral ICAO not only affects the occluded side but also triggers regional redistribution of CBF in the contralateral hemisphere to compensate for cerebral ischemia. This finding was not recognized in the past because of the lack of detailed segmentation of brain regions.

In our current study, patients with internal ICAO presented with a spectrum of clinical manifestations ranging from asymptomatic to TIA to small infarcts within the MCA territory. Despite similar vascular occlusions, outcomes vary significantly on the basis of the ability to recruit collateral pathways that restore blood flow to the ischemic region during the minutes and hours after an acute event[9,11]. Collateral blood flow plays a crucial role in steno-occlusive ICA disease by preventing irreversible ischemic damage[3]. All patients in this study received collateral compensation, either through the primary pathway of the circle of Willis or secondary pathways involving the leptomeningeal and ophthalmic arteries or through neovascularization. Different clinical manifestations indicate that the quality of collateral status varies widely in patients with ICAO. A previous study suggested that the collection of secondary collateral is related to more severe damage, and its existence might be viewed as a marker of insufficiency of the primary collateral routes[28,29]. Owing to the limited sample size in this study, we were unable to explore collateral circulation extensively or assess differences in CBF according to symptoms, which will be a critical direction for future research.

Due to the limited sample size in our study, caution is warranted when interpreting and generalizing the current results to other populations. Future studies will continue to accumulate larger samples to increase the robustness and applicability of the findings. The CBF measured in our study primarily reflects a combination of regional brain grey and white matter. It is known that CBF values differ between grey and white matter, with generally lower CBF values observed in white matter than in grey matter[11]. Therefore, the CBF values reported in our study may be lower than those reported in previous studies that focused predominantly on grey matter[16]. However, this difference does not compromise the reliability of our findings. Nevertheless, our results hold clinical significance by providing a foundational understanding for further research and informing clinical therapeutic strategies.

CONCLUSION

In conclusion, unilateral ICAO results in hypoperfusion in the global and MCA territories, affecting most ASPECTS areas on the occluded side. The ACA territory was not significantly affected. Perfusion deficits were also observed in some ASPECTS areas on the nonoccluded side. Using a single PLD of 1.5 seconds underestimates regional CBF; dual PLD settings prove more suitable for accurate CBF quantification in ICAO cases.

FOOTNOTES

Author contributions: Ding D designed the research study; Zhang YY and Liang WB analyzed the data; Zhang GR analyzed the data and wrote the manuscript. All authors have read and approve the final manuscript.

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